

CONTROL

Gender Differences in Perception of Dyspnea, Assessment of Control, and Quality of Life in Asthma

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Background. There is limited information on the inter-relationship between gender, perception of dyspnoea and health-related quality of life (HRQoL) in asthma. **Methods.** In a cross-sectional study in an out-patient setting, 85 patients with bronchial asthma, 41 males and 44 females, underwent spirometry and were administered the following instruments to measure asthma control, HRQoL and dyspnoea: (a) Asthma control questionnaire (ACQ), (b) Asthma Quality of Life questionnaire (AQLQ), (c) Baseline dyspnoea index (BDI) questionnaire and Oxygen Cost Diagram (OCD). **Results.** Overall, male patients had greater airways obstruction but reported similar level of asthma control as females. Among patients with mild persistent asthma, females had a poorer level of control. The BDI and the OCD scores were significantly lower in female patients indicating greater dyspnoea and they also had a poorer quality of life especially in the symptoms and emotional domains of the AQLQ. After adjusting for the severity of airways obstruction in multivariate analysis, female gender and a poorer quality of life were independent predictors of increased perception of dyspnoea. **Conclusions.** Female patients with asthma are likely to have a greater perception of dyspnoea, report a poorer control and have a poorer quality of life as compared to males. Female gender and a poorer quality of life are independent predictors of increased perception of dyspnoea in asthmatics.

Keywords asthma, asthma control, dyspnea, gender differences, quality of life

Both epidemiological and clinical studies in asthma suggest remarkable gender differences. The reported differences include a higher prevalence among males before puberty, reversing later to a female predominance (1–3), a greater increase over time in prevalence and mortality due to asthma among women than in men (4), and a greater prevalence of bronchial hyperresponsiveness (5) and health care utilization including emergency room visits and hospitalizations among women (6, 7). These observations may have a hormonal basis as there is some evidence that the effect of estrogens on cells involved in asthma is pro-inflammatory while testosterone has opposing effects (8, 9). These studies may also suggest that asthma may be more severe in women. This, however, is not established as gender differences in hospitalization rates were found to disappear when differences in prevalence were taken into account (10). Further, outcomes of acute exacerbations of asthma have been reported to be similar in males and females (11).

Patient-centered outcomes including dyspnea and health-related quality of life (HRQoL) are increasingly being used as outcome parameters in management. Studies suggest that women may have a greater perception of dyspnea than men with similar or even lesser degrees of airways obstruction (12–14). They may also have a more negative impact of the disease in terms of a poorer quality of life (13, 15–17). In these studies,

either subjective self-reported or categorical measures were used for dyspnea assessment or it was evaluated as one of the domains of a quality of life scale. None of the above studies have used a more comprehensive quantitative measure of dyspnea. Further in these studies, the reported gender differences in perception of dyspnea have not been examined in relation to differences in quality of life. Recent guidelines have shifted focus from evaluation of severity to assessment of control in day-to-day management of asthma (18). As control assessment by the physician and the patient is largely symptom-based, perception of dyspnea would be a critical determinant of control and may affect its evaluation. We hypothesized that gender-related differences in perception of dyspnea should impact assessment of control and quality of life in asthma.

MATERIALS AND METHODS

A cross-sectional study was carried out in an outpatient setting. Consecutive patients above 18 years of age and diagnosed to have bronchial asthma were included after informed consent. The diagnosis was established on the basis of symptoms suggestive of asthma, documentation of airways obstruction, and a significant response to bronchodilators as defined in the Global Initiative for Asthma (GINA) guidelines (19). Smokers, those with a clinical and laboratory evidence of any other respiratory disorder or systemic disease, recent hospitalization (last 6 weeks) for an acute exacerbation of bronchial asthma, with pregnancy among females, and unwilling patients were excluded. All the patients were on treatment

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with inhaled corticosteroids and if required, long-acting beta agonists. The study protocol was approved by the Institutional Ethics Committee.

Sample size calculations were based on the reported ranges of the Baseline Dyspnea Index (BDI) (20). With $\alpha = 0.05$ and power of 80%, for detecting a difference of 1 unit in means between gender groups with an expected standard deviation of 1.5 units, a sample size requirement of 37 in either group was calculated.

Study Design

After enrollment, a detailed history was taken and general and systemic examination was carried out. Complete details regarding patient's demographics including education, marital status, duration of illness, employment, and socioeconomic status were noted. In addition, the menstrual history was obtained in females and the study was carried out in the first half of the menstrual cycle to avoid any confounding effect of premenstrual asthma that usually occurs in the second half.

After spirometry, all patients responded to the following interviewer-based reliable and validated instruments to measure asthma control, HRQoL, and dyspnea. These included the following: (a) Asthma Control Questionnaire (ACQ) (21); (b) Asthma Quality of Life Questionnaire (AQLQ) (22); and (c) dyspnea measurement by BDI questionnaire (20) and Oxygen Cost Diagram (OCD) (23).

The degree of asthma control was assessed by using the Hindi version of ACQ developed by Juniper et al. (21). The ACQ has six questions on symptoms and bronchodilator use that are measured on a 7-point scale (0 = no impairment, 6 = maximum impairment). The percentage of forced expiratory volume in 1 s ($FEV_1\%$) predicted is also scored on a 7-point scale as the seventh item of the ACQ. Patients are asked to recall how their asthma has been during the previous week. The ACQ score is the mean of the seven questions and therefore ranges between 0 (totally controlled) and 6 (severely uncontrolled). The HRQoL was assessed using the Hindi version of Juniper's AQLQ (22). It consists of 32 items that are divided into four domains: activity limitation, symptoms, emotional function, and environmental stimuli. Patients are asked to think about how they have been during the previous 2 weeks and to respond to each of the 32 questions on a 7-point scale (7 = not impaired at all to 1 = severely impaired). The overall AQLQ score is the mean of all 32 responses and the individual domain scores are the means of the items in those domains. Higher scores indicate a better quality of life. The BDI provides a multidimensional numerical quantitation of dyspnea. Described and validated by Mahler et al. (20), it has been extensively used in literature as an objective measure of dyspnea. It not only scores the magnitude of the task that provokes dyspnea but also rates the magnitude of the effort involved as well as the consequent functional impairment. It thus provides a more comprehensive assessment of dyspnea. It consists of five specific grades (0–4) scored by the interviewer for each of the three domains: magnitude of effort,

magnitude of task, and functional impairment. A total score is obtained by adding the three domain scores. Greater the score, the lower is the degree of dyspnea. The OCD is a visual analog scale consisting of a line 100 mm long with descriptive phrases at various points along the line that correspond to oxygen requirements of different activities. The top of the vertical line represents "no breathlessness" while the bottom of the line reflects "the greatest breathlessness" (23). The patient is asked to mark a point on the vertical line above which he or she became breathless. A shorter distance on the vertical 100 mm scale indicates greater limitation of routine activities due to dyspnea.

The sequence of tests was decided by lots. The technique of usage of metered-dose inhaler was assessed using the 10-point Manzella scale (24). Access to health care was assessed by Chang's questionnaire (25) which consists of five items related to ease of access to health care in the past 6 months. These latter scales were used as the technique of inhalation as well as access to health care may affect the attainment of control as well as the quality of life.

All patients underwent spirometry after overnight withdrawal of bronchodilators. Spirometry was performed on the dry rolling seal spirometer of a computerized apparatus (Benchmark model; P. K. Morgan and Co. Ltd., Kent, UK). The tests were performed according to the guidelines of the American Thoracic Society (ATS) (26). At least three acceptable and reproducible maximal expiratory flow volume loops were obtained. Forced vital capacity (FVC) and FEV_1 were recorded. Prediction equations for north Indian population were used (27).

Statistical Analysis

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS Inc., USA) 11 and GraphPad Prism 4.01 software (Graphpad Software Inc., La Jolla, CA, USA). The data were initially examined for the normality of distribution and homogeneity of variance. Between-group comparisons were carried out using Student's unpaired *t*-test or Mann-Whitney *U*-test as applicable. Proportions were evaluated using the chi-square test. Interaction between gender and severity as determinants of quality of life measures was carried out using multivariate analysis of variance. Pearson correlation coefficients were computed for bivariate relationships. Multiple linear regression was carried out to determine the relationship of dyspnea (as BDI scores) with gender adjusting for HRQoL and severity of airways obstruction. A value of 0.05 for α was considered as significant.

RESULTS

In all, 85 patients were included in the study. There were 41 males and 44 females. The demographic details and other characteristics of the patients are shown in Table 1. The age, proportions of patients with mild, moderate, and

TABLE 1.—Patient characteristics.

	Males	Females
Age	29.34 ± 8.05	26.57 ± 6.930***
Height	165.68 ± 6.49	154.22 ± 5.87**
Weight	59.85 ± 12.61	52.52 ± 9.629*
Duration of asthma (years)	9.20 ± 7.27	8.84 ± 8.48***
Severity (GINA)***		
Mild persistent	10 (24.4%)	19 (43.2%)
Moderate persistent	13 (31.7%)	11 (27.3%)
Severe persistent	18 (43.9%)	14 (29.5%)
Positive family history of asthma or rhinitis	16 (39.0%)	21 (47.7%)***
Presence of rhinitis	22 (53.7%)	19 (43.2%)***
Access to health care (Chang's score)	4.66 ± 0.71	4.78 ± 0.52***
Manzella score for use of inhalation device	88.10 ± 12	84.3 ± 11.22***

Notes: GINA, Global Initiative for Asthma.

P-values: *** $p > .05$ (not significant); ** $p < .001$; * $p < .05$.

severe persistent asthma, duration of disease, prevalence of allergic rhinitis and of family history of asthma or allergic rhinitis, access to health care, and scores for correctness of the technique of use of metered-dose inhalers were similar in the two groups ($p > .05$). Educational and economic status was also similar (data not shown).

The spirometry data and the level of control as evaluated by the ACQ are shown in Table 2. The FEV₁/FVC ratio and FEV₁% predicted were significantly lower in males while the level of asthma control was similar in the two genders. Comparing subgroups of similar asthma severity, the FEV₁/FVC ratio and FEV₁% predicted were significantly lower in males with moderate persistent asthma but the ACQ scores were similar. On the other hand, female patients had similar lung function but higher ACQ scores in the mild persistent group indicating a poorer control.

TABLE 2.—Lung function and asthma control.

	Males	Females
FVC% predicted	93.89 ± 14.07	98.83 ± 18.86*
FEV ₁ % predicted	75.02 ± 21.48	89.69 ± 24.99**
FEV ₁ /FVC	63.44 ± 14.09	71.94 ± 12.68**
FEV ₁ % predicted in GINA severity groups		
Mild persistent	97.21 ± 11.03	109.65 ± 15.75*
Moderate persistent	78.05 ± 6.89	86.9 ± 13.56**
Severe persistent	60.49 ± 21.6	64.8 ± 18.02*
ACQ scores	1.32 ± 0.89	1.26 ± 0.65*
ACQ scores in GINA severity groups		
Mild persistent	0.6 ± 0.25	1.00 ± 0.48**
Moderate persistent	1.32 ± 0.86	1.02 ± 0.51*
Severe persistent	1.72 ± 0.02	1.85 ± 0.63*

Notes: FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; GINA, Global Initiative for Asthma; ACQ, Asthma Control Questionnaire.

P-values: * $p > .05$ (not significant); ** $p < .01$.

The total BDI scores in female patients were lower (7.05 ± 2.1) than in males (8.39 ± 2.1) indicating a greater level of dyspnea ($p < .01$). They also had lower scores in each of the BDI domains compared to males: functional impairment, 2.36 ± 0.92 and 2.76 ± 0.8 ($p < .05$); magnitude of task, 2.32 ± 0.7 and 2.78 ± 0.8 ($p < .01$); and magnitude of effort, 2.36 ± 0.8 and 2.85 ± 0.8 ($p < .01$) (Figure 1). Comparing severity-wise, the BDI total and domain scores were significantly lower in female patients in mild and severe persistent asthma but not in the moderate persistent group (Table 3). The OCD score was significantly lower in females than in males (60.09 ± 15.5 and 68.44 ± 15.6 , respectively, $p < .05$) overall as well as in each category of asthma severity (Table 3).

Females had lower total AQLQ scores as compared to males (35.35 ± 5.5 and 37.96 ± 7.5 , respectively, $p < .05$) and also in the symptoms (53.43 ± 10.4 and 58.73 ± 12.9 , respectively, $p < .001$) and emotional domains (18.68 ± 5.9 and 24.78 ± 5.8 , respectively, $p < .01$) indicating that they had a poorer quality of life. However, in activity limitation and environment domains the differences were not statistically significant (Figure 2). Comparisons according to asthma severity revealed lower total and all domain scores in females in mild persistent asthma but no gender differences in moderate persistent asthma. In severe persistent asthma, females had lower scores in total as well as in the symptoms and emotion domains (Table 3).

The correlations of BDI and OCD scores with total AQLQ and domain scores are shown in Table 4. Both BDI and OCD scores had significant correlations with the total as well as each of the four AQLQ domains in both male and female patients. Further, as the AQLQ total and domain scores showed gender differences as well as a steady decline with increasing severity of asthma, the interaction between gender and asthma severity in their effects on quality of life was also examined by multivariate analysis of variance. Significant main effects were revealed for gender ($F = 9.58$, $p < .001$) and severity of asthma ($F = 20.08$, $p < .01$). However, there was no significant interaction between gender and severity of asthma indicating that these had independent effects on the quality of life. Finally, a multivariate linear regression model confirmed gender as an independent predictor of BDI after adjusting for quality of life and severity of airways obstruction. In the model, gender (categorical with males=1, females=2) had a standardized β of -0.203 ($p < .05$) and total AQLQ had a standardized β of 0.614 ($p < .001$) with adjusted r^2 being 0.47. The model predicted that a female patient will have lower BDI scores (greater dyspnea) after controlling for quality of life and severity of airways obstruction.

DISCUSSION

The present study shows that female patients with asthma experience greater dyspnea, report a poorer control, and

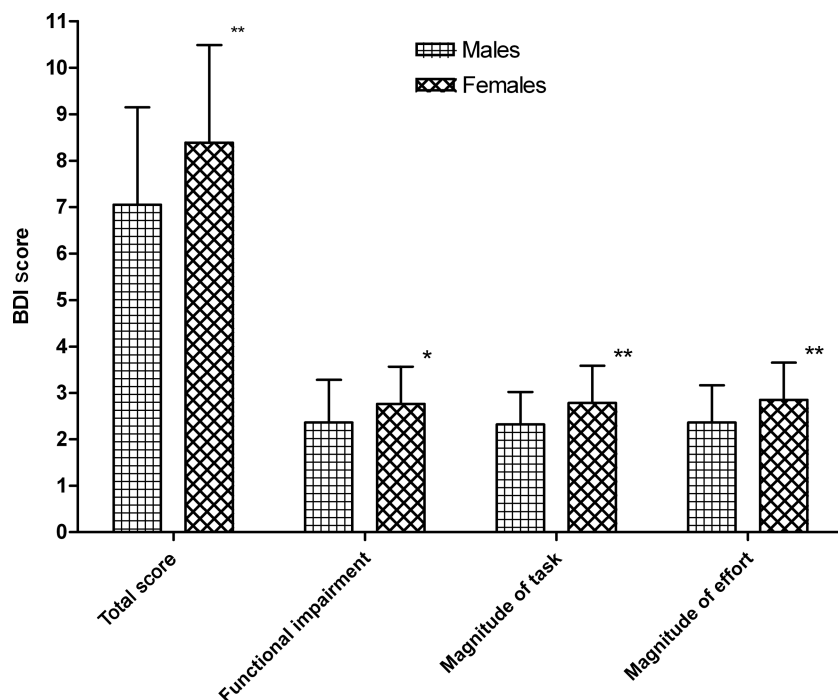


FIGURE 1.—Total and domain scores of the Baseline Dyspnea Index (BDI) in male and female patients.

Note: * $p < .05$, ** $p < .01$.

TABLE 3.—Baseline Dyspnea Index (BDI), Oxygen Cost Diagram (OCD), and Asthma Quality of Life Questionnaire (AQLQ) scores according to GINA severity.

	Mild persistent asthma		Moderate persistent asthma		Severe persistent asthma	
	Males	Females	Males	Females	Males	Females
BDI total	10.2 ± 0.9	8.11 ± 1.7**	8.46 ± 1.5	7.82 ± 1.5***	7.33 ± 2.3	5 ± 1.6*
BDI functional impairment	3.6 ± 0.5	2.79 ± 0.8**	2.69 ± 0.6	2.64 ± 0.7***	2.33 ± 0.8	1.57 ± 0.8**
BDI magnitude of task	3.2 ± 0.4	2.63 ± 0.5**	2.77 ± 0.6	2.64 ± 0.5***	2.56 ± 0.9	1.64 ± 0.5**
BDI magnitude of effort	3.4 ± 0.5	2.68 ± 0.6**	3 ± 0.6	2.55 ± 0.5***	2.44 ± 0.9	1.79 ± 0.9**
OCD	79.4 ± 0.8	70.00 ± 12.8*	71.85 ± 0.3	59.91 ± 9.7**	59.89 ± 17.7	46.79 ± 12.6**
AQLQ total	43.58 ± 3.8	37.79 ± 4.4**	39.63 ± 7.36	37.12 ± 4.8***	33.64 ± 6.7	30.13 ± 3.8***
AQLQ symptoms	68.90 ± 4.8	56.05 ± 10**	60.85 ± 14.5	59.42 ± 8.7***	51.56 ± 10.9	44.08 ± 5.1*
AQLQ activity limitation	58.80 ± 4.9	53.26 ± 5.9*	53.38 ± 7.1	49.33 ± 6.5***	45.33 ± 10.5	45.38 ± 7.1***
AQLQ emotional function	28.20 ± 2.5	20.95 ± 6.3**	25.08 ± 6.1	20.83 ± 4.2***	22.67 ± 6.1	13.38 ± 2.9**
AQLQ environmental stimuli	23.40 ± 1.7	20.89 ± 3.4*	19.23 ± 5	18.92 ± 4.8***	15.56 ± 4.9	17.69 ± 2.7***

Notes: GINA, Global Initiative for Asthma.

P-values: *** $p > .05$ (not significant); ** $p < .01$; * $p < .05$.

have a poorer quality of life as compared to male patients with similar GINA-defined severity of asthma. The gender differences in asthma control were independent of differences in lung function impairment. Male patients had greater airways obstruction but similar ACQ scores as females whereas the latter had a poorer level of control as compared to the former in the subset of mild persistent asthma with matched lung function.

As the ACQ takes into account the frequency and severity of symptoms, the subjective perception of

symptoms is likely to affect the overall score. The ACQ enquiry on the use of need-based rescue bronchodilators reflects patient behavior in response to symptoms and thus should be influenced by the degree of his/her tolerance. Our observations suggest either a greater tolerance of airways obstruction among males or a greater perception of the same among females or both. Poorer scores in the symptoms domain of the AQLQ in female patients as compared to male patients with similar GINA-defined severity confirmed these gender differences in perception.

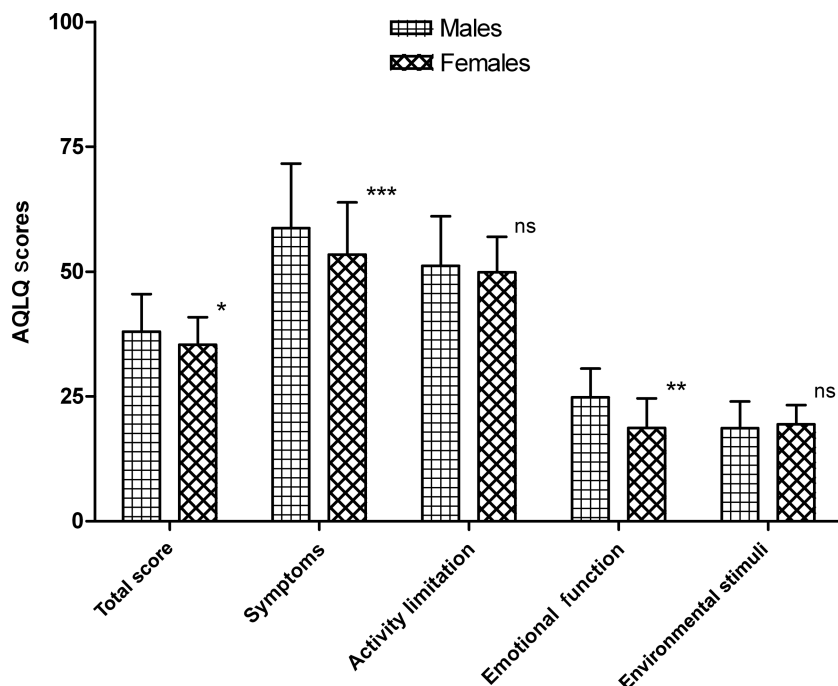


FIGURE 2.—Total and domain scores of the Asthma Quality of Life Questionnaire (AQLQ) in male and female patients.

Note: * $p < .05$; ** $p < .01$; *** $p < .001$; **** $p > .05$ (not significant).

TABLE 4.—Correlations of BDI and OCD scores with AQLQ scores.

AQLQ score	BDI		OCD	
	Males	Females	Males	Females
Total	0.64***	0.70***	0.59***	0.76***
Symptoms	0.72***	0.67***	0.63***	0.63***
Activity limitation	0.63***	0.52***	0.64***	0.63***
Emotional function	0.44**	0.57***	0.39*	0.62***
Environmental stimuli	0.5**	0.39***	0.39*	0.49**

Notes: BDI, Baseline Dyspnea Index; OCD, Oxygen Cost Diagram; AQLQ, Asthma Quality of Life Questionnaire.

P-values: *** $p < .001$; ** $p < .01$; * $p < .05$.

The symptoms domains of the AQLQ and the ACQ measure the same construct. The gender differences in perception may explain the greater healthcare utilization by female asthmatics reported in previous studies (6, 7). On the other hand, male patients may be undertreated because of poorer perception or greater tolerance. With the recent shift in focus in management from severity to control, gender differences in perception of symptoms need to be taken into account while planning the treatment. This aspect has hitherto not been addressed in management guidelines.

Belloch et al. (17) using the AQLQ reported an overall poorer quality of life in women with intermittent asthma and in the emotional domain in the mild and moderate persistent asthma. Wijnhoven et al. (13) using a disease-specific and a generic instrument observed that except in the 35–55 years age group, younger and older women had a poorer quality of life. Osborne et al. (16)

found that after matching with male patients for severity of airways obstruction, women had more symptoms and also a poorer quality of life in most of the subscales of the Short Form-36 and asthma-specific quality of life questionnaires. Our results are in agreement with these studies. However, unlike Belloch et al. (17), we found significant gender differences over a wider range of severity of asthma and in several domains of AQLQ. Interestingly, the gender differences in quality of life were independent of the severity of asthma, suggesting subjective differences in perception, affective response, and coping skills.

Several studies have shown that women experience greater dyspnea for the same or even better level of airways function and perceive a worsening of symptoms better than males (12–14). Cydulka et al. (14) remarked that either women are more likely to report more frequent and intense symptoms and have activity limitation or males may have a greater tolerance. This may explain why women with asthma are prescribed more medicines than men for similar level of severity (28) and pay more frequent visits to their physicians (13). In the multiple regression model in this study, we showed that female patients experience greater dyspnea after adjusting for quality of life and severity of airways obstruction. Thus, our results confirm and extend the observations of the earlier studies.

A greater degree of anxiety and depression have been documented in women (17) and these were noted to appear at comparatively milder degrees of severity of asthma as compared to men (29). Women are also prescribed sedatives and tranquilizers three times more frequently than age- and severity-matched asthmatic

males (28). In the current study, we found that female patients fared worse in the AQLQ emotions domain indicating a greater psychological impact of the disease.

Although inter-patient differences in perception of dyspnea among asthmatics have been reported earlier (30, 31), this is the first study to report gender differences in perception. Weiner et al. (32) have suggested that differences in perception of dyspnea among asthmatics may relate to inspiratory muscle strength. However, in the present study, female gender and poor quality of life but not severity of airways obstruction were found to be significant predictors of increased perception of dyspnea, and thus a role for non-mechanical factors is suggested. The sensation of dyspnea involves central cortical processing of information from the respiratory center and peripheral receptors, and is modulated by psychological, behavioral, and cultural factors that determine a person's ability to perceive the stimulus and respond to it. This perception is a complex behavioral phenomenon that imparts to dyspnea its subjective quality (33). Gender differences are probably due to these subjective factors.

Our results may have been confounded by possible differences in management, compliance, access to health care, environmental exposures, and socioeconomic and cultural factors. Care was taken to account for some of these influences. The standard of care was similar (19). While female patients have been reported to make more errors in the inhalation technique (34), in our study both genders used the inhalers equally well, likely a result of patient education in our clinic. Chafin et al. (35) also found no gender differences in the inhalation technique when patients were trained beforehand. Economic and educational status and access to health care were similar in both genders. The confounding effect of premenstrual aggravation of asthma was avoided by studying female patients in the first half of the menstrual cycle. However, other factors such as knowledge, attitudes, practices, adherence to prescribed treatment, and differences in occupational and environmental exposures may yet confound the outcomes.

CONCLUSIONS

Female patients with asthma have a greater perception of dyspnea, report a poorer control, and have a poorer quality of life as compared to male patients with matched severity of asthma. These reflect greater suffering and poorer coping skills among females. Female gender and a poorer quality of life are independent predictors of increased perception of dyspnea in asthmatics. These observations have important clinical implications. Management strategies should take cognizance of these gender differences.

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DECLARATION OF INTEREST

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